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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,270	08/03/2001	Jurgen Kleinschmidt	31304-704.831	3472

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WILSON SONSINI GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 943041050

EXAMINER	
WINKLER, ULRIKE	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,270	KLEINSCHMIDT ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14 and 16* is/are allowed.

6)☒ Claim(s) *13, 15 and 17-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 25, 2005 has been entered.

The rejection of claims 13 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Bett et al. (Proceeding of the National Academy of Science, 1994) **is withdrawn** in view of applicants amendments to the claims. The amendments now make it clear that the nucleic acid sequence contemplated by the invention is a single nucleic acid sequence made up of two components. The first component is the adeno-associated virus nucleic acid sequence. By claiming a nucleic acid sequence this implies that more than one nucleotide is needed in order to be as sequence. The amendment now does not read on a single nucleic acid. However, the amendment does not make it clear how much of the sequence is required. The second component is the helper virus sequence that is defined in the claim as comprising the complete adenovirus 5 sequence having a deletion in either the E1 or the E1 and L1 region. The prior rejection is withdrawn because the claims no longer read on a single nucleotide from the AAV sequence.

The rejection of claims 13, 17-20 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bett et al. (Proceeding of the National Academy of Science, 1994) and Colosi (U.S. Patent No. 6,004,797) **is withdrawn** in view of applicants amendments to the claims. The cited references do not provide motivation to include both adenovirus and adeno associated viral sequences on a single plasmid.

New rejections in view of the amendments to the claims:

Claims 13, 15, 17, 20-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In this instance the claim are rejected because the specification fails to describe what nucleic acid structures are included or excluded from (1) the adeno-associated virus (AAV) nucleic acid and (2) rAAV.

The specification indicates that the full-length AAV sequence is 4680 nt. In the examples the only 4235 nt of the AAV sequence is introduced into the plasmid containing the adenovirus sequence. There is a discrepancy of 445 nt between the AAV sequence that is inserted into the adenovirus containing plasmid and the whole AAV sequence. The claims as written require an AAV sequence indicating that more than one nucleotide is required but the claims to not define how much of the AAV sequence is need and as written can include the entire sequence. It is clear from the specification that the AAV sequences contemplated do not include the entire AAV genome yet the claims do not reflect this and could include the entire AAV sequence.

The specification does not make it clear what is encompassed by rAAV. On page 2, line 24 of the specification the "rAAV vector commonly present in cells." If AAV is found in cell and the genome normally is integrated into chromosome 19 of a cell. Only in the presence of helper virus is the virus able to escape from the cell. rAAV is nowhere defined in the specification. It is not clear what AAV sequences are present in the rAAV construct and what sequences are present in the plasmid construct comprising the AAV and adenovirus sequences. Page 3, lines 3-5 "the expression of "rAAV vector" comprises any AAV viral particle [this would read on wild type] and its DNA, which may [does not equal must] contain foreign DNA, except for that of the helper virus, which is necessary to develop AAV particles." This definition does not provide any insight as to what nucleic acid structures encompass rAAV because it could read on a wild type AAV virus. The next explanation in the specification does not help either see page 4, lines 9-10, "..the rAAV viral particle preparations distinguish themselves in that they contain no AAV wild type sequences." What does it mean to contain no wild-type sequences? Does this contemplate using AAV ITRs that are not found in wild type virus?

Applicants need to define what is encompassed by (1) the adeno-associated virus (AAV) nucleic acid and (2) rAAV. Applicants need to distinctly claim the subject matter that they regard as their invention.

The following claim suggestion is made in order to overcome the claim deficiency for the adeno-associated virus (AAV):

> A nucleic acid sequence comprising an adeno associated virus (AAV) nucleic acid sequence and an AAV helper virus nucleic acid sequence, wherein said AAV helper virus sequence comprises the complete adenovirus 5 sequence with the exception of the E1 region, wherein said AAV nucleic acid sequence comprises AAV rep gene, AAV cap gene, AAV p19 promoter, AAV p40 promoter and replacing AAV p5 promoter with a heterologous promoter.

The above is a mere suggestion for potential claim clarification purposes. Applicant is not required to use the suggestion. Applicant is reminded that any amendment to the claims must be supported by a written description in the specification; it is applicants' obligation to ensure the proper support is indeed present. Applicants also need to ensure that there are no problems with antecede basis in the suggested claims. The suggestions made by the examiner has not been checked for support in the specification.

Claims 17 are 20-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not provide a written description of what is encompassed by the rAAV structure. A review of the art indicates that rAAV is not a standard definition and therefor the art cannot substitute as providing written description of the term and what is included in the rAAV structure. No single definition of what is encompassed by the term rAAV is found in the specification. On page 2, line 24 of the specification the "rAAV vector commonly present in cells." AAV is found in cell and the genome normally is integrated into chromosome 19 of a cell. Only in the presence of helper virus is the virus able to escape from the cell. rAAV is nowhere define in the specification. It is not clear what AAV sequences are present in the rAAV construct. Page 3, lines 3-5 "the expression of "rAAV vector" comprises any AAV viral particle [this would read on wild type] and its DNA, which may [does not equal must] contain foreign DNA, except for that of the helper virus, which is necessary to develop

AAV particles." This definition does not provide any insight as to what nucleic acid stuctures are contemplated as encompassing rAAV because it could read on a wild type AAV virus. The next explanation in the specification does not help either see page 4, lines 9-10, "..the rAAV viral particle preparations distinguish themselves in that they contain no AAV wild type sequences." What does it mean to contain no wild-type sequences? Does this contemplate using AAV ITRs that are not found in wild type virus? The claims are rejected for lack of written description.

Claims 20-27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: inserting the rAAV nucleic acid construct into the cell. It is not clear from the specification where the rAAV structures come from, they could either be already part of the cell and integrated into the gene or they could be transfected into the cell at the same time the AAV/AD5 nucleic acid construct is inserted into the cell

Claims 17 are 20-27 are objected to because of the following informalities: The claims use abbreviations such as "rAAV" the compound should be spelled out before the first use of the abbreviation. Appropriate correction is required.

Conclusion

Claims 13, 15, 17-27 are rejected.

Claims 14 and 16 are allowable; the claims are allowable as written because they make reference to a specific sequence. The plasmids have been deposited in a recognized depository

under the Budapest Treaty as evidenced by the declaration by Dr. mult zur Hausen provided October 30, 2001.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PH.D.
PRIMARY EXAMINER 4/29/05